JAPANESE DERMATOLOGICAL ASSOCIATION
THE JOURNAL OF DERMATOLOGY
doi: 10.1111/j.1346-8138.2011.01418.x
Journal of Dermatology 2012; **39**: 527–530

ORIGINAL ARTICLE

Health-related quality of life assessed by the effect of bepotastine besilate in patients with pruritus: Importance of emotions score in atopic dermatitis

Tamihiro KAWAKAMI, Satoko KIMURA, Tsuneo HAGA, Risako DOI, Mikiko KYOYA, Keiko NAKAGAWA, Yoshinao SOMA

Department of Dermatology, St Marianna University School of Medicine, Kawasaki, Japan

ABSTRACT

The Skindex-16 questionnaire was recently developed as a measure of dermatological health-related quality of life (HRQoL), including symptoms, emotions and functional aspects. Bepotastine besilate is a selective histamine H_1-receptor antagonist and a second-generation non-sedating antihistamine to treat various dermatological disorders. We assessed changes of the HRQoL instrument (Skindex-16) on patients with pruritus, including those with atopic dermatitis (AD) over bepotastine treatment period. The patients' personal assessment of the intensity of pruritus was determined using the Visual Analog Scale (VAS) for pruritus. Patients answered the Skindex-16 at baseline and at week 4. Forty-eight of 51 enrolled dermatological patients completed the Skindex-16. Of the 48 patients, 11 had AD and 37 had other conditions. Improvement in the clinical evaluation and VAS score was significant in all patients, the AD group and the other disorders group between baseline and week 4. Skindex-16 showed significantly lower scores for each of the three scales (symptoms, emotions and functioning) and the global score at baseline compared to that at week 4 in all patients and the other disorders. In contrast, there was a significant reduction in the emotions and global score among the AD patients. We found a significant correlation between falls in emotions score of Skindex-16 and falls in VAS scores for pruritus in the AD group. Bepotastine could be effective in the management of patients' HRQoL and useful in patients suffering with pruritus. We suggested that pruritus of AD patients could exert a stronger emotional effect due to the skin condition compared to the symptomatic or functional effects.

Key words: atopic dermatitis, bepotastine besilate, emotions, health-related quality of life, pruritus, Skindex-16.

INTRODUCTION

Itching arises from a variety of skin conditions.[1,2] Particularly, itching is the predominant feature of atopic dermatitis (AD) and it is an essential diagnostic feature of the disease.[3,4] Learning more about how itching affects people may help us develop better treatment strategies for dermatological patients with pruritus. Histamine H_1-receptor antagonists (antihistamines) are used to treat various dermatological disorders including urticaria, eczema and AD.[5] Bepotastine besilate is a selective histamine H_1-receptor antagonist and a second-generation, non-sedating antihistamine that has recently been used for the treatment of allergic disorders in Japan.[6]

Health-related quality of life (HRQoL) has emerged as an important outcome of clinical investigation and patient care in dermatology.[7] The Skindex has been recently developed as a specific measure of HRQoL in dermatology patients, quantifying the effects of skin disease on patients' HRQoL, which has been extensively studied and refined. Initially, the Skindex was comprised of 61 questions but was then modified to 29 questions. Later, a briefer version consisting of 16 questions was introduced, which is known as Skindex-16.[8–10] The Skindex-16 is a self-administered questionnaire covering symptoms, emotions and functional aspects of dermatological conditions. Four questions (nos. 1–4) are related to symptoms, seven questions (nos. 5–11) are related to emotions, five questions (nos. 12–16) are related to functioning, and all 16 questions are related to global score. We assessed changes of the HRQoL instrument (Skindex-16) on patients with pruritus, including those with AD, over a bepotastine treatment period.

METHODS

Patients

Fifty-one Japanese patients suffering from pruritus and above the age of 20 years seen at the Department of Dermatology,

Correspondence: Tamihiro Kawakami, M.D., Ph.D., Department of Dermatology, St Marianna University School of Medicine, 2-16-1 Sugao, Miyamae-ku, Kawasaki, Kanagawa 216-8511, Japan. Email: tami@marianna-u.ac.jp
Funding sources: None.
Conflict of interest disclosure: None declared.
Received 15 August 2011; accepted 5 September 2011.

St Marianna University School of Medicine between 2008 and 2010 were eligible for the study. Exclusion criteria were specific pruritus treatments that patients were currently taking or had received in the last 3 months. These treatments included phototherapy, antihistamines, corticosteroids, immunosuppressive drugs, or any other experimental or investigational drug. Patients gave written informed consent prior to the start of the study. Dermatological disorders were diagnosed by experienced dermatologists based on the Japanese Dermatological Association criteria. The diagnosis of AD was defined by the Hanifin and Rajka[11] diagnostic criteria.

Forty-eight of the 51 enrolled patients with pruritus completed the Skindex-16 questionnaire and the results of bepotastine treatment were followed over the course of 4 weeks. Of the 48 patients (26 men, 22 women; aged 55.6 ± 21.9 years), 11 (23%) had AD (six men, five women; aged 27.1 ± 10.8 years) and 37 (77%) had other conditions (20 men, 17 women; age 64.1 ± 16.4 years). In the other disorder group, 10 patients were diagnosed with cutaneous pruritus of unknown origin, eight with urticaria, seven with prurigo chronica and seven with chronic eczema. The mean duration of their disorder was 46.9 ± 78.3 months for all 48 patients, 135.6 ± 118.9 months for the AD group and 19.2 ± 25.8 months for the other disorder group. The ages and duration of disorder differed significantly between the AD group and the other disorders group.

Methods

All 51 patients with associated pruritus who enrolled in the study were treated with an oral non-sedating H_1 antihistamine, bepotastine besilate 10 mg, twice daily (morning, evening) for 4 weeks. The patients continued using any topical corticosteroid and/or emollient they were currently using during the 4 weeks. Clinical evaluation for pruritus was graded as "none", "mild", "moderate", "severe" or "very severe" according to same dermatologists who examined the patients with pruritus at baseline and at week 4. All adverse events were recorded throughout the study from the time of patient consent to the final visit. The patients similarly reported on the intensity of pruritus at baseline and week 4 using the Visual Analog Scale (VAS) for pruritus.[12,13] Patients graded their pruritus using a 10-cm VAS, with "none" on the left side of the scale and "severe" on the right. All patients answered the Skindex-16 questionnaire at baseline and at week 4. HRQoL was assessed using the Skindex-16 questionnaire, which consists of 16 items within three scales: symptoms, emotions and functioning. Patients answered each question using a 7-point scale from 0–6 (0 = "never bothered" and 6 = "constantly bothered"). The mean score was determined for each scale. The global score was calculated by averaging the mean scores for each item. Further details of scoring are provided in previous publications.[10] The questionnaire was distributed to each patient, and they submitted them to the clerks in our clinic on the same day.

Statistical analysis

The level of significance was set at $P < 0.05$ in all cases. Mann–Whitney *U*-test was performed to define the patient's background between two patient groups, the AD group and the group with other disorders. Clinical evaluations for pruritus assessed by dermatologists at baseline and week 4 were analyzed by Wilcoxon rank sum tests. The statistics were analyzed by paired Stucent's *t*-test to compare VAS scores for pruritus and Skindex-16 scores among all patients, the AD group and the other disease group. Spearman's rank correlation coefficients were used to compare the difference between the Skindex-16 scores and VAS scores for pruritus. All data are expressed as the mean ± standard deviation.

This study was based on the ethical principles of Good Clinical Practice and was approved by the St Marianna University School of Medicine Institutional Review Board for Human Subjects Research (no. 1427).

RESULTS

Clinical evaluation and VAS scores for pruritus

Clinical evaluation for pruritus assessed by dermatologists over bepotastine treatment period improved significantly in all 48 patients, the AD group and the other disease group (Fig. 1). There were no reported adverse affects during bepotastine treatment. VAS scores (27.3 ± 26.0) for pruritus assessed by each patient at week 4 were significant lower than the baseline score (60.7 ± 20.1) in all 48 patients with pruritus. VAS scores (34.5 ± 25.5) for pruritus at week 4 were significantly lower than the baseline score (60.5 ± 17.1) in the AD group. VAS scores (25.1 ± 26.1) for pruritus at week 4 were significantly lower than the baseline score (60.7 ± 21.1) in the other disease group. There was no significant difference in VAS scores for pruritus between the AD group and the other disorder group.

Changes in Skindex-16 scores

All 48 patients who completed the Skindex-16 questionnaire showed significantly lower scores for each of the three scales (symptoms, emotions and functioning) and the global score at baseline compared to that at week 4 (Fig. 2). This indicates an improvement in HRQoL among the pruritus patients who underwent

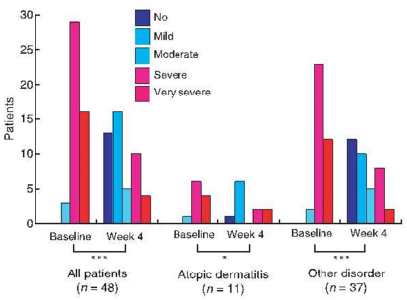

Figure 1. Clinical evaluation of pruritus assessed by dermatologists over bepotastine treatment period was significant in all patients, the atopic dermatitis group and the other disease group using Wilcoxon rank sum tests. ***$P < 0.001$, *$P < 0.05$.

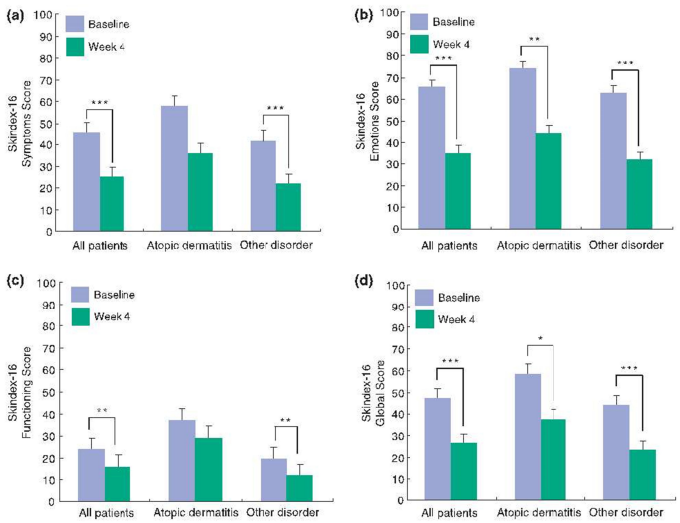

Figure 2. Skindex-16 questionnaire in symptoms score (a), emotions score (b), functioning score (c) and global score (d) at baseline and week 4 among all patients, the atopic dermatitis (AD) group and the other disorder group. ***$P < 0.001$, **$P < 0.01$, *$P < 0.05$.

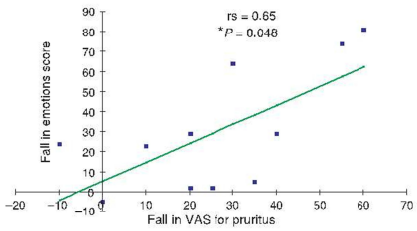

Figure 3. We found significant correlation between falls in emotions score of Skindex-16 and falls in Visual Analog Scale (VAS) score for pruritus among the atopic dermatitis group who underwent bepotastine treatment using Spearman's rank correlation coefficients.

bepotastine treatment. This same trend was seen among the other disorder group, where there was a significant reduction in four Skindex-16 scores between baseline and week 4 (Fig. 2). In contrast, the symptoms and functioning scores in the AD group did not decrease significantly between baseline and week 4 (Fig. 2a,c). However, there was a significant reduction in the emotions and global score among the AD patients (Fig. 2b,d). Furthermore, we found a significant correlation between falls in emotions score of Skindex-16 and falls in VAS scores for pruritus in the AD group (Fig. 3).

DISCUSSION

In the present study, the pruritus of our patients who received bepotastine to treat their itching improved from both the dermatologists' and patients' point of view. Skin disease-specific, the Skindex-16 HRQoL instrument is valuable for assessing patients' outcomes, especially their response to therapy. These improvements were noted against the three scales (symptoms, emotions and functioning) of the Skindex-16 questionnaire, in addition to global scores of the Skindex-16 questionnaire over the treatment period. We suggest that bepotastine could be effective in the management of patients' HRQoL and useful in patients suffering with pruritus.

Both clinical evaluation for pruritus by dermatologists and VAS scores for pruritus by patients significantly improved in the AD group after 4-week administration of bepotastine. Some investigated whether the Skindex-16 could measure disease severity and clinical change in the estimation of the effects of AD on patients' HRQoL.[14,15] The Skindex-16 questionnaire showed significantly lower scores for both emotions score and global score at baseline compared to that at week 4 in the AD group. We found that falls in the emotions score significantly correlated with falls in VAS scores for pruritus. Based on these data, we suggest that pruritus of AD

patients could exert a stronger emotional effect due to the skin condition compared to the symptomatic or functional effects, as indicated by the high scores on the emotional component of the Skindex-16 in pruritus patients with AD. Therefore, emotional impact could be an important measure of HRQoL in AD patients. Due to scratching, the primary skin disease may be confounded by secondary scratch lesions. This may occur in excoriated forms of AD. Acute phases in AD are primarily characterized by extreme pruritus, which in turn leads to excoriation. Excoriation further exacerbates the underlying inflammation, setting up an itch–scratch cycle, resulting in chronic lesions.[16] Bepotastine has favorable antihistamine properties leading to allergic inflammation beyond those directly involving the histamine H_1-receptor.[17] It is important for dermatologists to effectively treat the underlying causes of emotion associated with pruritus in AD patients. We expect that the results of our questionnaire analysis may provide some basis for dermatologists to effectively assess HRQoL in the treatment regimen for AD.

ACKNOWLEDGMENTS

This work was supported by grants from the Scientific Research Fund of the Ministry of Health, Labor and Welfare, Japan (Grant-in-Aid for Scientific Research, Research on Allergic disease and Immunology (H20-004).

REFERENCES

1 Ständer S, Weisshaar E, Mettang T *et al.* Clinical classification of itch: a position paper of the International Forum for the Study of Itch. *Acta Derm Venereol* 2007; **87**: 291–294.
2 Lovell P, Vender RB. Management and treatment of pruritus. *Skin Therapy Lett* 2007; **12**: 1–6.
3 Stander S, Steinhoff M. Pathophysiology of pruritus in atopic dermatitis: an overview. *Exp Dermatol* 2002; **11**: 12–24.
4 Dawn A, Papoiu AD, Chan YH, Rapp SR, Rassette N, Yosipovitch G. Itch characteristics in atopic dermatitis: results of a web-based questionnaire. *Br J Dermatol* 2009; **160**: 642–644.
5 Sidbury R. Systemic therapy of atopic dermatitis. *Clin Exp Dermatol* 2000; **25**: 559–566.
6 Nakahara T, Urabe K, Moroi Y, Morita K, Furue M. Bepotastine besilate rapidly inhibits mite-antigen induced immediate reactions in atopic dermatitis. *J Dermatol Sci* 2003; **32**: 237–238.
7 Abeni D, Picardi A, Pasquini P, Melchi CF, Chren MM. Further evidence of the validity and reliability of Skndex-29: an Italian study on 2242 dermatological outpatients. *Dermatology* 2002; **204**: 43–49.
8 Chren MM, Lasek RJ, Sahay AP, Sands LP. Measurement properties of Skindex-16: a brief quality of life measure for patients with skin diseases. *J Cutan Med Surg* 2001; **5**: 105–110.
9 AlGhamdi KM, AlShammari SA. Arabic version of Skindex-16: translation and cultural adaptation, with assessment of reliability and validity. *Int J Dermatol* 2007; **46**: 247–253.
10 Higaki Y, Kawamoto K, Kamo T, Horikawa N, Kawashima M, Chren MM. The Japanese version of Skindex-16: a brief quality-of-life measure for patients with skin diseases. *J Dermatol* 2002; **29**: 693–698.
11 Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol Suppl (Stockh)* 1980; **92**: 44–47.
12 Kawakami T, Kaminishi K, Soma Y, Kushimoto T, Mizoguchi M. Oral antihistamine therapy influences plasma tryptase levels in adult atopic dermatitis. *J Dermatol Sci* 2006; **43**: 127–134.
13 Imaizumi A, Kawakami T, Murakami F, Soma Y, Mizoguchi M. Effective treatment of pruritus in atopic dermatitis using H1 antihistamines (second-generation antihistamines): changes in blood histamine and tryptase levels. *J Dermatol Sci* 2003; **33**: 23–29.
14 Higaki Y, Kawamoto K, Kamo T, Ueda S, Arikawa J, Kawashima M. Measurement of the impact of atopic dermatitis on patients quality of life: a cross-sectional and longitudinal questionnaire study using the Japanese version of Skindex-16. *J Dermatol* 2004; **31**: 977–982.
15 Kawashima M, Harada S. Effect of standard medication on quality of life of patients with atopic dermatitis. *J Dermatol* 2007; **34**: 9–16.
16 Wahlgren CF. Itch and atopic dermatitis: an overview. *J Dermatol* 1999; **26**: 770–799.
17 Williams JI, Gow JA, Klier SM, McCue SL, Salapatek AM, McNamara TR. Non-clinical pharmacology, pharmacokinetics, and safety findings for the anthistamine bepotastine besilate. *Curr Med Res Opin* 2010; **26**: 2329–2338.